

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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| In re the Application of |) | Examiner: DAVIS, Minh Tam B |
| Ming-Fong Lin et al. |) | Art Unit: 1642 |
| Serial No.: 09/919,196 |) | Response to Paper No. 7 |
| Filed: July 31, 2001 |) | |
| For: "NOVEL PROSTATE CANCER |) | |
| CELL LINES" |) | |

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DECLARATION OF MING-FONG LIN

I, Ming-Fong Lin, hereby declare that:

1. I am a United States citizen residing at 327 South 92nd Street, Omaha, NE 68114.

2. I received a Bachelor of Science degree from School of Pharmacy, Kaoshiung Medical College, Kaoshiung, Taiwan in 1974, an M.S. degree from Institute of Molecular Biology, National Tsing Hua University, Hsingchu, Taiwan in 1976, and a Ph.D. degree from Roswell Park Memorial Institute Graduate Division, State University of New York at Buffalo, New York in 1983. Additional details of my educational background are set forth in my *Curriculum vitae*, attached hereto.

3. From February 1983 to February 1986, I was a Postdoctoral Associate under the supervision of Dr. G.M. Clinton, at Department of Biochemistry, Louisiana State University Medical Center, New Orleans, LA. From March to December of 1996, I held a position as Research Assistant Professor at Department of Biochemistry and Molecular Biology, LSU Medical Center, New Orleans, LA. I was a Research Assistant Professor at Department of Biochemistry, The Oregon

Health Sciences University, Portland, OR from January 1987 to July 1988; an Assistant Professor at Department of Urology, USC School of Medicine, Los Angeles, CA from August 1988 to May 1995; an Associate Professor at the Eppley Institute for Research in Cancer and Allied Diseases, University of Nebraska Medical Center (UNMC), Omaha, NE from May 1996 to June 2000; and an Associate Professor at Department of Biochemistry and Molecular Biology and Section of Urologic Surgery, UNMC, Omaha, NE from May 1995 to June 2000. I have been an Attending Research Scientist (WOC status) at Omaha VA Hospital, Omaha, NE and a Coordinator of UNMC Prostate Cancer Research Focus Group since 1996. I have also been a Member of the UNMC/Eppley Cancer Center, UNMC, Omaha, NE since October of 1995. Currently, I also hold a position of Professor at Department of Biochemistry and Molecular Biology, Section of Urologic Surgery, College of Medicine, and the Eppley Institute for Research in Cancer and Allied Diseases, UNMC, Omaha, NE. Additional details of my professional history are set forth in my *Curriculum vitae*.

4. I have over 30 years scientific training and research experience in the areas of biochemistry, molecular biology, urology and cancer research. I am the author or co-author of 53 scientific publications, 3 book chapters or Review articles, 42 abstracts, 35 presentations in International or National conferences and meetings, 23 invited presentations, 6 presentations at UNMC, and 3 pending scientific publications. I am also the inventor or co-inventor of 2 pending U.S. Patent Applications. Details are set forth in my *Curriculum vitae*.

5. My current research interests include investigation into the signal transduction pathway involved in regulation of cell proliferation. A more thorough understanding of the signals which lead to aberrant cell growth and proliferation will provide new clinically relevant targets for interfering

with this process.

6. I am the sole inventor of the invention described and claimed in U.S. Patent Application Serial No. 09/919,196, entitled "Novel Prostate Cancer Cell Lines" (referred to hereinafter as "the present application"), claims 1-4 of which are currently under rejection in the U.S. Patent and Trademark Office.

7. I have read and am familiar with the Official Action dated January 27, 2003, in the present application. I understand that the Examiner has rejected claims 1-4 as the specification allegedly lacks enablement for a NE-like cell line, such as NE-1-3, NE-1-8, or NE-1-9 stored in any medium. As the principle investigator in the discovery of human prostate cancer-associated neuroendocrine (NE)-like cell lines, and as the sole inventor of the subject matter of the present application, I completely disagree with the Examiner, for the reasons set forth in the following paragraphs

8. The NE-like cell lines disclosed in the present application are composed of "terminally differentiated" cells. The biochemical properties and the phenotype are irreversible, since the NE phenotype is maintained even after long-term culture in both hormone-deficient and hormone-containing medium. Data supporting this assertion are provided in Figure 1, attached hereto.

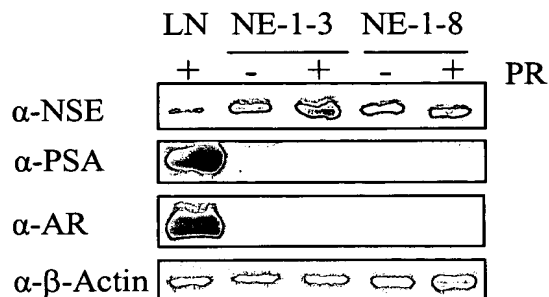


Figure 1. Human prostate cancer cell line LNCaP, human prostate cancer-associated NE-like cell lines NE-1-3 and NE-1-8 were cultured in regular medium (+), i.e., phenol red (PR)-positive RPMI-1640 medium containing 5% FBS, or in a steroid-reduced medium (-), i.e., phenol red (PR)-negative RPMI-1640 medium containing 5% charcoal/dextran-stripped FBS for 3 months. Cells were harvested and analyzed, respectively, by western blotting for the expression of NSE, a marker for NE cells, and PSA and AR, markers for LNCaP cells. β -actin was used as a control for loaded amounts in each sample.

9. As illustrated in Figure 1, the instantly claimed NE-cell lines, e.g., NE-1-3 and NE-1-8, maintain the expression of NSE, a marker for NE cells, after culturing in both steroid-reduced and steroid containing medium for 3 months.

10. It is therefore, submitted that the human prostate cancer-associated NE-like cell lines of the present invention are irreversibly differentiated NE-like cell lines which can be maintained and propagated in any type of medium without losing their NE phenotype.

I hereby further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed true; and further that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of

the United States Code, and that such willful statements may jeopardize the validity of the above-referenced application or any patent issued thereon.

DATE

7/28/2003

Ming-Fong Lin

A handwritten signature in dark ink, appearing to read 'Ming-Fong Lin', written over a horizontal line.